

revised in response to the Examiner's rejections and to better clarify the claims as described below.

The amendments should not be construed as an acquiescence to the rejections and have been made solely to expedite the prosecution of this application. Applicants reserve the right to pursue the previous claims in another application(s). The amendments do not add any new matter.

Section 112, First Paragraph Rejections

Claims 26, 29, 31, 42-55, 75-86, 95-106 and 108-115 were rejected under §112, first paragraph, the Examiner stating that the specification describes sequences which are "in excess of" 70% identical to the amino acid sequences set forth in SEQ ID NO:4 or SEQ ID NO:6, rather than "at least" 70% identical to those sequences. The claims have been amended to include the "in excess of" terminology which was used in the specification at page 20, line 9, to describe the preferred polypeptides. Therefore, the rejection may properly be withdrawn.

The Examiner then states that the material incorporated by reference to Dayhoff which describes this determination of identity is deemed to be essential material regarding alignment. The Dayhoff material is disclosed in the specification at page 20, lines 12-21, wherein the alignment and comparison of sequences for the determination of percent identity is described. While the material is already disclosed in the specification, including the description of the inclusion of gaps in compared sequences, the Dayhoff material is further specifically incorporated by means of the Declaration Regarding Material Incorporated by Reference (M.P.E.P. 608.01(p)) which accompanies this response and which amends the specification. No new matter has been added with the amendment to the specification.

Claim 26 (new claim 117) was also rejected on the assumption that the hybridization conditions described in the examples (such as Example 2) do not provide a basis for the description of hybridization using conditions of "reduced stringency". Applicants respectfully submit that the disclosure of conditions in the specification, which are clearly and completely described as conditions of reduced stringency, fully supports the use of the claim terminology "conditions of reduced stringency" to describe the hybridizing conditions. Those skilled in the art know that there are a variety of condition variables that can be manipulated to provide conditions of reduced stringency. It is not necessary or practical, nor desired by the Patent

Office, that an applicant include every possible set of conditions when these are well known in the art (please see Beltz *et al.* (*Methods in Enzymology* 100:266-285, 1983), Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*, 2nd edition) and Lathe, *J. Mol. Biol.*, 183, 1-12 (1985) which have previously been made of record in this case.) To facilitate prosecution, however, the claim has been amended to identify the conditions of reduced stringency that were used (see Example 2) to provide a completely clear example of suitable conditions that may be used. With this amendment, the rejection should properly be withdrawn.

The basis for claim 29 (new claim 122) is the description of pre-pro forms of glial cell line-derived neurotrophic factor. A pre-pro sequence for GDNF is depicted in SEQ ID NO:25. It is clear that pre-pro residues described in the specification (see for example page 8, lines 1-6) may precede the amino acid sequence of GDNF.

Claims 110, 112 and 113 have been canceled in favor of the revised claims which render the objections moot. Claim 50 (new claim 143) was amended to delete the amplification language just as it was previously deleted from claim 44.

Claims 95-98, 101 and 108-112 were objected to for not including identified steps and terminology (such as culturing, expressing and isolating) as found in the preceding and allowed claims. The claims have been revised as described above to particularly include such steps and traditional claim terminology as found in claims 50 and 86 (new claims 143 and 149, respectively) as suggested by the Examiner. Thus the claims clearly and particularly describe the recombinant production of GDNF, and therefore, the earlier rejection may properly be withdrawn.

Claim 116 (new claim 158) was rejected under §112, as non-enabling. New claim 158 depends from and further characterizes the factor expressed by the nucleic acid sequences of claim 117. Applicants respectfully submit that the previous rejection is rendered moot with the revisions.

Section 112, Second Paragraph Rejections

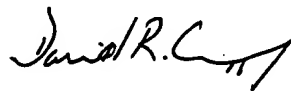
Claim 107 (new claim 135) was rejected under §112, second paragraph as indefinite. The claim now clearly points out the recombinant modification of a host cell to express

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particularly claimed nucleic acid sequences. In addition, the claim is distinct from that of the other host cell claims with the particular and different identification of the sequences which may be expressed.

For the foregoing reasons and in view of the amendments, Applicants respectfully request reconsideration of and withdrawal of the outstanding rejections. Applicants' representative would appreciate the opportunity to talk with the Examiner, in person, to discuss any remaining questions and facilitate the prosecution of the application.

Respectfully submitted,



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